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10/736,112	12/15/2003	Jeffrey S. Ross	M2051-700410	5668

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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	

NOTIFICATION DATE	DELIVERY MODE
04/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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DETAILED ACTION

The amendment of 03/19/08 is not and will not be entered, because it requires new search for SEQ ID NO:1 and SEQ ID NO:2, which are introduced into the specification.

The following are answers to the response arguments.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-16, 33-34 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons already of record in paper of 09/21/07.

The response asserts that claim 1 has been amended to recite "a reference standard that is statistically significant between subjects diagnosed with prostate cancer and having recurrence and subjects diagnosed with prostate cancer that do not have recurrence". The response asserts that reference standard is PSMA expression levels in a primary tumor of a subject diagnosed with prostate cancer that does not have recurrence. The response asserts that as shown in, for example, Perner et al. and Ross et al. (cited in the previous reply), the meaning of statistically significant is clear to one of ordinary skill in the art. The response asserts that one of skill in the art could, using standard statistics, determine statistically significant differences between expression levels of a given protein between the two patient populations. The response asserts that as demonstrated by the references cited in the previous reply, this is not a relative term.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains, because the amendment is not and will not be entered. Further, in previous response to 112, second paragraph, Perner and Ross were not recited. The term "statistically significant" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Further, it is not clear what constitutes a reference standard.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-16, 33-34 remain rejected under 35 U.S.C. 112, first paragraph, for lack of a clear written description of PSMA, for reasons already of record in paper of 09/21/07.

The response asserts that the amendment has obviated the rejection.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains, because the amendment is not and will not be entered.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1, 3-16, 33-34 remain rejected under 35 U.S.C. 112, first paragraph, for lack of enablement of a method for determining risk of prostate cancer recurrence, by detecting an increased PSMA level of expression, for reasons already of record in paper of 09/21/07.

1. Essential material

The claims and the specification were amended to recite SEQ ID NO:1 and SEQ ID NO:2.

Rejection remains, because the amendment is not and will not be entered.

2. Determination of risk of prostate cancer recurrence

Concerning the issue that it is unknown "whether such data of Perner et al could be used for predicting recurrence in an unknown population of treated patients, who are in remission.", the response asserts that since the amended claims require determining PSMA levels in a sample from a **primary** tumor of **a patient having prostate cancer**, the claims do not cover analyzing a subject in remission for PSMA levels.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains, because the amendment is not and will not be entered.

The response asserts that Tockman et al and Vandesompele et al are analyzing proteins as predictive markers for early detection of primary cancers and not for recurrence in a patient population diagnosed with a cancer, as amended in the claims. The response asserts that the

amended claims require the sample be from the primary tumor whereas both Beckett et al. and Thomas et al. were analyzing serum for circulating PSMA levels, and thus Beckett et al. and Thomas et al. are not relevant.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains, because the amendment is not and will not be entered.

The response asserts that the only remaining reference cited by the Office as contradictory is Bostwick et al. published ten years ago. The response asserts that in addition to the two exhibits cited in the previous reply, Applicants attach an additional post filing exhibit (Cytogen Press Release, dated May 22, 2006) that support Applicants' finding that PSMA expression levels in primary tumor samples predict prostate cancer recurrence. The response asserts that in fact, Applicants were unable to find any evidence since Applicants' invention that contradicted Applicants' findings. The response asserts that inn view of the overwhelming evidence to support Applicants' finding (in contrast to the one ten year old reference cited by the Office), there is sufficient guidance provided in the present application to enable to claimed invention.

The response has been considered but is not found to be persuasive for the following reasons:

The exhibit by Cytogen, 2006, is not considered because the amendment is not and will not be entered.

Further, concerning Bostwick et al, although it is published in 1998, there is no evidence that the data in Bostwick et al, which also have statistical analysis of prostate cancer recurrence 6.9 years after radical prostatectomy, are false and could be refuted by the claimed invention, nor by Perner et al.

Thus, the need for validation of a maker for its predictive value in a prospective population trial, as taught by Tockman, applies as well to the instant application, especially in view of contradictory results in the art, concerning the predictive value of PSMA.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-6, 11-16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al, 1998 (Urology, 51: 89-97), for reasons already of record in paper of 09/21/07.

The response asserts that Murphy et al. disclose analyzing circulating PSMA levels from serum samples. The response asserts that nothing from the Murphy et al. reference teaches or suggests that PSMA expression levels in the primary tumor of a subject having prostate cancer, as now claimed in the amended claims, can assess the patient's risk for recurrence in the future.

The response has been considered but is not found to be persuasive for the following reasons:

Rejection remains, because the amendment is not and will not be entered.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH-TAM DAVIS
April 23, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643